



Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-021

Bristol-Myers Squibb Pharmaceutical Research Institute
Attention: Warren Randolph
Director, Worldwide Regulatory Affairs
P.O. Box 4000
Princeton, NJ 08543-6000

AUG 17 1998

APPROVED FOR

Dear Mr. Randolph:

Please refer to your supplemental new drug application dated January 16, 1998, received January 22, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pravachol (pravastatin sodium) Tablets.

This supplemental new drug application provides labeling changes to the INDICATIONS AND USAGE, CONTRAINDICATIONS, PRECAUTIONS, and REFERENCES sections of the Pravachol package insert. These changes include:

APPROVED

INDICATIONS AND USAGE

A footnote has been added to the NCEP Guidelines, "In CHD patients with LDL-C levels 100 to 129 mg/dL, the physician should exercise clinical judgement in deciding whether to initiate drug treatment."

A statement has been added following the NCEP Guidelines, "At the time of hospitalization for an acute coronary event, consideration can be given to initiating drug therapy at discharge if the LDL-C level is ≥ 130 mg/dL (see NCEP Guidelines, above)."

CONTRAINDICATIONS

The word "immediately" has been inserted to modify when the drug should be discontinued in the case of pregnancy. A cross-reference to "PRECAUTIONS: Pregnancy" has been added to this section.

PRECAUTIONS

Under "Information for patients", a cross-reference to "WARNINGS: Skeletal Muscle" has been added.

Under "Pregnancy", text pertaining to animal findings with another HMG-CoA reductase inhibitor has been deleted, as has that pertaining to a woman who received another HMG-CoA reductase inhibitor and dextroamphetamine during the first trimester of pregnancy.

"Rare reports of congenital anomalies have been received following intrauterine exposure to other HMG-CoA reductase inhibitors. In a review⁷ of approximately 100 prospectively followed pregnancies in women exposed to simvastatin or lovastatin, the incidences of congenital anomalies, spontaneous abortions and fetal deaths/stillbirths did not exceed what would be expected in the general population. The number of cases is adequate only to exclude a three-to-four fold increase in congenital anomalies over the background incidence. In 89% of the prospectively followed pregnancies, drug treatment was initiated prior to pregnancy and was discontinued at some point in the first trimester when pregnancy was identified. As safety in pregnant women has not been established and there is no apparent benefit to therapy with Pravachol during pregnancy (see CONTRAINDICATIONS), treatment should be immediately discontinued as soon as pregnancy is recognized" has been inserted.

REFERENCES

A reference, Manson et al. (1996) has been added; this is the review which is summarized in PRECAUTIONS.

We have completed the review of this supplemental application and it is approved. The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert dated January 16, 1998) with the revisions approved in supplements 18, 19 and 20. Marketing the product with FPL that is not identical to the approved labeling text described above may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-898/S-021." Approval of this submission by FDA is not required before the labeling is used.

If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

If a letter communicating important information about this drug product (i.e., a "Dear Healthcare Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6430.

Sincerely,

/s/ 3/14/88

Solomon Sobel, M.D.

Director

Division of Metabolic and Endocrine Drug Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

cc:

Archival NDA 19-898

HFD-510/Div. Files

HFD-510/M. Simoneau

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-102/ADRA (with labeling)

HFD-40/DDMAC (with labeling)

HFD-613/OGD (with labeling)

HFD-95/DDMS (with labeling)

HFD-820/DNDC Division Director

DISTRICT OFFICE

Drafted by: Mas/July 31, 1998

Initialed by: D.Orloff 7.31.98/W.Berlin 8.3.98/S.Moore 8.3.98/R.Steigerwalt 8.3.98/E.Galliers 8.4 and 8.14.98

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APPROVAL (AP)